ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclix 250 µg/ml solution for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Cloprostenol 250 µg
as Cloprostenol sodium 263 µg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	20 mg
Citric Acid Monohydrate (as a pH adjuster)	
Sodium Citrate	
Sodium Chloride	
Sodium Hydroxide (as a pH adjuster)	
Water for injections	

Colourless solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (cows).

3.2 Indications for use for each target species

Induction of luteolysis allowing resumption of oestrus and ovulation in cyclic females when used during dioestrus, synchronisation of oestrus (within 2 to 5 days) in groups of cyclic females treated simultaneously, treatment of suboestrus and uterine disorders related to a functioning or persistent corpus luteum (endometritis, pyometra), treatment of ovarian luteal cysts, induction of abortion until day 150 of pregnancy, expulsion of mummified foetuses, induction of parturition.

3.3 Contraindications

Do not use in pregnant animals, for which induction of abortion or parturition is not intended.
Do not use in animals with spastic diseases of the respiratory or gastrointestinal tract.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:
As with parenteral administration of any substance, basic aseptic rules should be observed. The injection site must be thoroughly cleaned and disinfected in order to reduce the risk of infection with anaerobic bacteria.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to benzyl alcohol should avoid contact with the veterinary medicinal product.
Do not eat, drink or smoke while handling the veterinary medicinal product.
Direct contact with skin or mucous membranes of the user should be avoided. Prostaglandins of the $F_{2\alpha}$ type may be absorbed through the skin and may cause bronchospasm or miscarriage. The veterinary medicinal product must be handled carefully to avoid ACCIDENTAL SELF-INJECTION OR SKIN CONTACT. Pregnant women, women in childbearing age, asthmatics and persons with other respiratory tract diseases should exercise caution when handling cloprostenol. Those persons should wear rubber (or plastic) gloves during administration of the veterinary medicinal product. Accidental spillage on the skin should be washed immediately with soap and water.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle (cows):

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic-type reaction *
Undetermined frequency (cannot be estimated from the available data):	Injection site infection ** Retained placenta ***

* Anaphylactic-type reactions can be observed which might be life threatening and require rapid medical care.
** Anaerobic infection if anaerobic bacteria penetrate the tissue at injection site, in particular following intramuscular injection.
*** When used for induction of parturition and dependent on the time of treatment relative to the date of conception, the incidence of retained placenta may be increased.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing

authorisation holder or its local representative or the national competent authority via the national reporting system. See also the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
Do not use in pregnant animals, for which abortion or induction of parturition is not intended.

Lactation:
The veterinary medicinal product can be safely used during lactation.

3.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of oxytocin and cloprostenol increases effects on the uterus. The activity of other oxytocic agents can be increased after the administration of cloprostenol.

Do not use in animals being treated with non-steroidal anti-inflammatories, as the synthesis of endogenous prostaglandins is inhibited.

3.9 Administration routes and dosage

Intramuscular use.

For all indications, 0.5 mg cloprostenol/animal corresponding to 2 ml of the veterinary medicinal product, injected intramuscularly.

In order to synchronise oestrus in groups of females, it is recommended that the veterinary medicinal product is administered on two occasions with a between treatment interval of 11 days.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Therapeutic tolerance in cattle is broad. Overdoses of more than 10 times are generally well tolerated. Large overdoses may cause transient diarrhoea. No antidotes are available.
An overdose will not accelerate corpus luteum regression.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal: 2 days
Milk: Zero hours

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QG02AD90

4.2 Pharmacodynamics

The Prostaglandin F2α analogue cloprostenol has luteolytic activity. Following its administration plasma progesterone falls to baseline levels. Progesterone concentrations start to

decrease as early as 2 hours following injection. As a consequence, females with a sensitive CL (i.e. at least 5 days old) return to oestrus within 2-5 days of treatment and ovulate.
The effect of cloprostenol on the smooth muscular system is similar to that of Prostaglandin F2α itself.

4.3 Pharmacokinetics

Following intramuscular injection, cloprostenol is rapidly adsorbed and peak cloprostenol concentrations are generally reached within the first 15 minutes after injection. Blood cloprostenol concentrations steadily decrease with a mean half-life of approx. 56 min.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life of the veterinary medicinal product after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Keep the vial in the outer carton.
Protect from light.

5.4 Nature and composition of immediate packaging

20 ml and 50 ml colourless glass vials (glass type I, Ph.Eur.) closed with a halogenobutyl rubber stopper, with or without teflon coating.
An aluminium crimp cap with an integral plastic tamper-evident cover is fixed over the rubber stopper.
Secondary packaging: cardboard box.

Not all pack sizes may be marketed

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

9 DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.
Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box containing a vial of 20 ml or 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclix 250 µg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Cloprostenol 250 µg/ml
as Cloprostenol sodium 263 µg/ml

3. PACKAGE SIZE

20 ml
50 ml

4. TARGET SPECIES

Cattle (cows)

5. INDICATION(S)

6. ROUTES OF ADMINISTRATION

Intramuscular use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 2 days
Milk: 0 hours

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened, use within 28 days.

Once broached, use by:

9. SPECIAL STORAGE PRECAUTIONS

Keep the vial in the outer carton.
Protect from light.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

VIRBAC

14. MARKETING AUTHORISATION NUMBER(S)

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of 20 ml or 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclix

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

250 µg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

1. Name of the veterinary medicinal product

Cyclix 250 µg/ml solution for injection for cattle

2. Composition

Each ml contains:

Active substance:
Cloprostenol 250 µg
as Cloprostenol sodium 263 µg

Excipients:
Benzyl alcohol (E1519) 20 mg

Colourless solution.

3. Target species

Cattle (cows).

4. Indications for use

Induction of luteolysis allowing resumption of oestrus and ovulation in cyclic females when used during dioestrus, synchronisation of oestrus (within 2 to 5 days) in groups of cyclic females treated simultaneously, treatment of suboestrus and uterine disorders related to a functioning or persistent corpus luteum (endometritis, pyometra), treatment of ovarian luteal cysts, induction of abortion until day 150 of pregnancy, expulsion of mummified foetuses, induction of parturition.

5. Contraindications

Do not use in pregnant animals, for which induction of abortion or parturition is not intended.
Do not use in animals with spastic diseases of the respiratory or gastrointestinal tract.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special precautions for safe use in the target species:
As with parenteral administration of any substance, basic aseptic rules should be observed. The injection site must be thoroughly cleaned and disinfected in order to reduce the risk of infection with anaerobic bacteria.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to benzyl alcohol should avoid contact with the veterinary medicinal product. Do not eat, drink or smoke while handling the veterinary medicinal product. Direct contact with skin or mucous membranes of the user should be avoided. Prostaglandins of the $F_{2\alpha}$ type may be absorbed through the skin and may cause bronchospasm or miscarriage. The veterinary

medicinal product must be handled carefully to avoid ACCIDENTAL SELF-INJECTION OR SKIN CONTACT. Pregnant women, women in childbearing age, asthmatics and persons with other respiratory tract diseases should exercise caution when handling cloprostenol. Those persons should wear rubber (or plastic) gloves during administration of the veterinary medicinal product. Accidental spillage on the skin should be washed immediately with soap and water.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy and lactation:
Do not use in pregnant animals, for which abortion or induction of parturition is not intended. The veterinary medicinal product can be safely used during lactation.

Interaction with other medicinal products and other forms of interaction:
Concurrent use of oxytocin and cloprostenol increases effects on the uterus. The activity of other oxytocic agents can be increased after the administration of cloprostenol.
Do not use in animals being treated with non-steroidal anti-inflammatories, as the synthesis of endogenous prostaglandins is inhibited.

Overdose:
Therapeutic tolerance in cattle is broad. Overdoses of more than 10 times are generally well tolerated. Large overdoses may cause transient diarrhoea. No antidotes are available.
An overdose will not accelerate corpus luteum regression.

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Cattle (cows):

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Anaphylactic-type reaction *
Undetermined frequency (cannot be estimated from the available data):
Injection site infection ** Retained placenta ***

* Anaphylactic-type reactions can be observed which might be life threatening and require rapid medical care.
** Anaerobic infection if anaerobic bacteria penetrate the tissue at injection site, in particular following intramuscular injection.
*** When used for induction of parturition and dependent on the time of treatment relative to the date of conception, the incidence of retained placenta may be increased.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system <{national system details}.>

8. Dosage for each species, routes and method of administration

Intramuscular use.

For all indications, 0.5 mg cloprostenol/animal corresponding to 2 ml of the veterinary medicinal product, injected intramuscularly.

9. Advice on correct administration

In order to synchronise oestrus in groups of females, it is recommended that the veterinary medicinal product is administered on two occasions with a between treatment interval of 11 days.

10. Withdrawal periods

Meat and offal: 2 days
Milk: 0 hours

11. Special storage precautions

Keep out of the sight and reach of children.
Keep the vial in the outer carton.
Protect from light.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and the outer carton. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Cardboard box with 1 x 20 ml or 1 x 50 ml vial.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}
Detailed information on this veterinary medicinal product is available in the Union Product Database (*https://medicines.health.europa.eu/veterinary*).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release:

VIRBAC
1ère avenue – 2065 m – LID
06516 Carros
FRANCE

Local representative(s) and contact details to report suspected adverse reactions: